RESEARCHES

ON THE NATURE OF

THE NORMAL DESTRUCTION OF SUGAR

IN THE

ANIMAL SYSTEM.

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In the last number of the late series of the 'Guy's Hospital Reports,' (October, 1853), we published a paper on the 'Physiological Relations of Saccharine Matter in the Animal Economy.' The expcriments that had been made up to that timc, enabled us to say but little concerning the *destruction* of sugar in the animal system. Indeed, the following passage (pp. 343, 344) will show the state of unecrtainty under whieh we wrote at that period. "There scems, therefore, something besides the mere chemical action of aeration requircd to effect the destruetion of saecharine matter in thc animal cconomy; but what this something is, remains yet to be dctermined by further experimental investigation." Sincc then, our researches have been continucd, and have led, we think, to the discovery of some important conelusions, which are advanced in the following communication, that may hence be regarded as the sequel of our previous publieation on this subject.

Saccharine and amylaccous substances form an exeeedingly largc constituent of the alimentary materials that are derived from the vegetable kingdom. When these are ingestcd or received into the alimentary traet, the former, is directly absorbed by thc venous radieles of the portal system, and conveyed to thc capillaries of the liver, whence it is poured

through the hepatic veins into the general circulatory system; whilst the latter, has previously to undergo a metamorphosis that seems effected by the aid of the salivary and pancreatic secretions, whereby it is converted into sugar, which, is then absorbed into the portal system, and similarly conveyed through the capillaries of the liver into the general circulation. Besides the supply of saccharine matter that is thus afforded by the ingested materials, M. Claude Bernard has shown, ('Nouvelle Fonction du Foie,' Paris, 1853), that the liver of all animals in a state of health is constantly manufacturing or producing a considerable quantity of this substance, which is also poured into the general circulation through the hepatic veins. The experiments conducted in M. Bernard's laboratory have also shown, that, not only does the liver of animals possess the power of forming sugar, but that, it exerts some modifying influence on that which is traversing its capillaries, and which has been absorbed from the food, by which, it is transformed from vegetable into animal sugar or glucose, and thus rendered more apt for being subsequently destroyed by the processes of animal life.

From the fact that animals are endowed with the capacity of abundantly forming this substance, whereby they are rendered, as it were, independent of its supply with the food from without, and from the consideration that it is present to a large extent in milk—the sole nutriment of young mammalia—it may, I think, be justly inferred, that saccharine matter should be looked upon as an exceedingly important if not an essential element of nutrition; and with these preliminary observations, we will at once direct our attention to the nature of the change or the metamorphosis that it undergoes, subsequently to its introduction into the circulatory system.

It having been stated, as the result of Bernard's experiments, that saccharine matter, whether derived from the food or formed by the hepatic organ, is constantly being poured into the general circulation through the hepatic veins; the first point that naturally suggests itself, is, to trace the blood onwards and determine if the sugar make its disappearance, and if so, in what part of the system this change is effected. From a great number of experiments conducted especially on

dogs and rabbits, I am able to affirm, what has been also observed in Paris, that whilst the blood contained in the right cavities of the heart is largely impregnated with sugar, that which is circulating in the arterial system or derived from the left ventricle, is almost destitute of this principle. From this it is evident, that a great portion of the sugar has undergone destruction during the transit of the blood through the pulmonary organs.

The difference of reaction communicated by the blood removed from the right and left side of the heart is always exceedingly striking and well marked; the one, after its colouring and albuminous constituents have been separated, giving an exceedingly abundant orange-yellow precipitate on ebullition with the copper test,[1] (Barreswil's solution); the other, similarly treated, merely a very small amount of yellowish precipitate, just sufficient to create a turbidity, which will vary slightly in intensity according to the period that has elapsed since the ingestion of food.

Although the sugar disappears to such an extent during the circulation of the blood through the capillaries of the respiratory organs, yet, after very numerous analyses, I may state,

[1] I may here briefly state the method that has been employed in searching for the presence of sugar in the animal solids and fluids. If it be a fluid, as for instance blood, that is to be examined, it is simply mixed with nearly an equal bulk of the pounded crystals of sulphate of soda, and exposed to the temperature of ebullition. The whole of the colouring and albuminous constituents are by these means precipitated, and a perfectly clear fluid runs through the filter, in which the slightest trace of sugar is easily recognised, by the aid of Barreswil's copper solution. With a solid, it is requisite that it should be cut into small pieces, and intimately pounded in a mortar with the sulphate of soda; the application of heat separates a limpid and transparent fluid, which may be obtained by filtration. The sulphate of soda, with which this clear fluid is saturated, does not at all interfere with the action of the test, that is subsequently employed. For the composition of the blue liquid of Barreswil (vide 'Guy's Hospital Reports,' Oct., 1853, p. 322). It is the test now always employed by Bernard in his experiments; and I may say, with regard to its action for the detection of the presence of sugar in blood and the animal solids, that I have now made several hundred analyses of these substances, and the uniform results that I have obtained induce me to speak in the strongest terms of confidence, respecting the accuracy and delicacy of this reagent. In the examination of specimens of urine, where there are only traces of sugar present, I am well aware that it does not react with the same facility; but in this case, there would seem to be certain saline ingredients also present, which have the effect of impeding its operation.

that I have never found it make an entire disappearance; arterial blood of the healthy animal, always remaining slightly impregnated, so as to communicate a sparing reaction to the test that is employed. And if the circulation of the blood be traced onwards through the general or systemic capillaries, the sugar will be found still to be undergoing a process of destruction; for, whilst arterial blood gives a more or less sparing reaction, that returned by the veins gives a still smaller one. But what appears to me exceedingly interesting (as having a bearing with reference to the *nature* of the destruction of sugar that I shall presently point out), is, that the blood returning from different parts of the system does not behave precisely alike as regards its saccharine qualities. For instance, having observed that the blood returning from such parts of the body as the head and neck or the extremities, always communicated, in my experiments, a traceable indication of the presence of sugar; whilst in other experiments, I had frequently found the blood in the portal vein perfectly free from saccharine impregnation; I was led to examine specimens of blood procured from the different veins of the same animal, and to discover, that, although the small quantity of sugar which escapes destruction in the lungs, and which remains to impregnate arterial blood, does not afterwards become entirely decomposed as it traverses the capillaries of the system at large, yet, that it makes a total disappearance in the blood circulating through the capillaries of the chylo-poietic viscera, *so as to leave that which is contained in the portal vein completely free from sugar*, *provided* none have been introduced into the alimentary canal with the food; *and provided, also,* the animal be not at a period of full intestinal digestion, when, as Bernard has pointed out, from the increased functional activity of the liver in forming sugar, the blood in every part of the system is more or less impregnated with this substance.

The details of the following experiment, which I have just performed at the period of writing this communication, is a repetition of others I have several times made, and will serve to show; not only, that the pulmonary organs form the chief seat of destruction of saccharine matter in the animal economy, but, that this process of destruction is also carried on in the general or systemic capillaries, especially those of the chylo-poietic

viscera, where, indeed, the sugar that escapes in the lungs may subsequently undergo a total or complete destruction.

Experiment.—In a good-sized dog, that had been living for three weeks past under my own observation, on animal food, I exposed the jugular and femoral veins, and removed a small quantity of blood from each. I next opened the femoral artery, likewise abstracting a small quantity of its contents; and, after sacrificing the animal by section of the *medulla oblongata*, I immediately made an incision through the abdominal parietes, placed a ligature on the portal vein just below its entrance into the liver, and collected a portion of the blood that was returning from the chylo-poietic viscera. The chest being opened and blood removed from the right ventricle of the heart, thus far completed the operating part of the experiment. The different specimens of blood that were thus procured were next carefully submitted to analysis, equal quantities of each being taken and exposed to precisely similar conditions. *That*, from the right side of the heart gave an abundant reaction with Barreswil's copper solution—a copious precipitate of the orange-yellow reduced oxide. *That*, from the femoral artery a slight reaction only; *that*, from the femoral and jugular veins still less, whilst the specimen of blood removed from the *vena portæ* communicated no reaction whatever. Upon the day of the experiment the animal had been fed as usual, about two hours and a half previous to the abstraction of the blood.

The *principal* seat of destruction of saccharine matter in the animal system, being thus experimentally shown to be located in the capillaries of the pulmonary organs, seems, at first sight, admirably to support the theoretical view propagated by Liebig, and entertained by most chemico-physiologists up to the present time, that sugar is one of those substances, which, undergoes a process of combustion in the animal economy, and which is resolved by the direct action of the oxygen absorbed during respiration into water and carbonic acid. It was to this view, that I, myself, inclined at the commencement of my inquiries, and my first experiments were directed in search of evidence to its support. It, indeed, occurred to me, that if the destruction of sugar in the lungs were owing to the direct chemical action of oxygen, on interfering with the respiratory process and

examining the effect produced on arterial blood, we ought to obtain a demonstrative proof of such a phenomenon. I therefore, in a healthy dog, cut down upon and exposed the carotid artery, and after abstracting a small quantity of its contents, which gave the usual slight saccharine reaction of arterial blood, I firmly ligatured a silver canula in the trachea, and partially plugged its orifice, so that the animal could only obtain an amount of air that was barely sufficient for the support of life. This soon induced a comatose condition, and in twenty minutes, or half an hour's time, I removed from the same vessel a second portion of blood, which was now almost black, and, therefore, of a perfectly venous character. On analysing this second portion of blood, it gave, it is true, a stronger reaction than the first, but the difference was nothing nearly what I had anticipated. For, on cutting off the supply of oxygen to such an extent, as that the blood should traverse the pulmonary capillaries without even becoming altered as regards its physical appearance, I certainly had expected, if the destruction of the sugar were owing to the cause attributed, to find the second specimen examined present scarcely any appreciable difference in reaction from the blood which is contained in the cavities of the right side of the heart. I have now repeated this experiment several times, and always with a similar result. I have also modified it, by causing the animal to respire hydrogen until death was nearly produced, and I still remained dissatisfied with the evidence that was afforded me. I, therefore, determined to push my investigations further, as I began to question, whether, there might not be some other cause in operation, in the living animal, to effect the normal destruction of sugar, besides the direct chemical action of the oxygen absorbed in respiration.

These investigations, which were first directed towards noticing the changes that were produced in blood containing sugar, injected through the capillaries of lungs removed from the animal, and artificially inflated with atmospheric air or oxygen gas,—I say, the results of these investigations led me, now some time since, to arrive at other conclusions relative to this subject. The views, which I have been induced to entertain entirely from my experiments on animals, refer the metamorphosis or destruction of sugar in the animal economy, as I

shall now proceed to show, to a process perfectly consistent and analogous with the well-known chemical bearings of this substance apart from the animal system.

In the following experiment, which I have now repeatedly performed, I have injected blood, removed from the right side of the heart of an animal—and therefore normally containing sugar—through the capillaries of the artificially inflated lungs of another; and it shows, in a most striking manner, the remarkable difference that is observable, in the action of oxygen on its saccharine constituent, *before* and *after* its spontaneous coagulation has taken place; or, in other words, *before* and *after* its vitality has been removed.

Experiment. Having sacrificed a middle-sized dog, by the destruction of its medulla oblongata, (a most ready means of occasioning instantaneous death,) I opened the chest, removed the contained viscera, and carefully washed away the blood from the interior of the heart and larger vessels. I next placed a canula, belonging to the syringe I intended to use in the experiment, in the right division of the pulmonary artery; and also arranged a small piece of glass tubing in the left auricle, so as to be enabled to collect the blood that should traverse the capillaries of the lung and issue through the right pulmonary veins. A tube, provided with a stop-cock, and communicating with a large bladder filled with atmospheric air, being firmly ligatured in the right bronchus, the corresponding lung was thus prepared for inflation and the injection of blood through its vessels, so as to imitate, as nearly as possible, the natural process of respiration. A much larger sized dog was now taken and sacrificed, in a similar manner, by pithing the medulla oblongata. The chest being quickly opened, and the heart exposed, a free incision was made into the right ventricle, and the blood collected in a vessel, from which a portion was immediately removed with the syringe, and slowly injected into the pulmonary artery of the lung that had previously been prepared and fully inflated with air. The blood traversed the pulmonary capillaries with but little resistance, and, issuing of a bright arterial hue through the tube placed in the left auricle, afterwards underwent the usual spontaneous coagulation.

On submitting equal quantities of the two specimens of

blood to analysis, and exposing them to precisely similar conditions; that, which remained in the syringe and had not traversed the pulmonary capillaries, gave the ordinary strong saccharine reaction of right ventricular blood; whilst that, which had been artificially subjected to the respiratory process, gave no more reaction than is usually observed in arterial blood removed from the living animal. Indeed, in one instance, in which the blood had been thus artificially arterialized, it communicated even a less reaction than is frequently met with in specimens of ordinary arterial blood.

From the details of this experiment, thus far conducted, we learn, that on injecting right ventricular blood—*immediately after its removal from the animal, and before spontaneous coagulation has taken place*—through the capillaries of a lung artificially inflated with atmospheric air, its saccharine constituent is as much metamorphosed or destroyed as if it had been circulating in the living animal. But, if we now continue the experiment, and operate on the blood that has separated from its fibrine, we shall find that a far different result is obtained.

The remaining portion of the blood collected from the incised right ventricle, having been placed in a vessel surrounded with warm water, so as to maintain its temperature equal to that in the living animal, was stirred with a glass rod, in order to separate its fibrin and leave the corpuscles mixed with the serum. The left lung of the first dog, having also been prepared in the same way as the right, and similarly inflated with air, the defibrinated blood, about half an hour after its removal from the animal, was injected, as previously, into the pulmonary artery, and readily issued through the pulmonary veins, presenting a highly arterialized colour.

The aërated and non-aërated portions of defibrinated blood that were thus obtained, were treated in a corresponding manner to the other specimens of blood procured in the first part of the experiment, and were *each of them* found to give the *same strong saccharine reaction* that was noticed in the right-ventricular blood examined immediately on removal from the animal.

Although, therefore, the saccharine element of the blood underwent such a marked decomposition, on being exposed to the influence of the air, before coagulation had taken place,

yet, subsequently to this process, not the slightest destruction was observed.

In the above experiment the lungs were inflated with atmospheric air, similar as employed in the normal process of respiration; but in others, I have substituted for air, oxygen gas and carbonic acid, and have also allowed the lungs to remain in a collapsed or non-inflated condition; and from the results of these modifications have found, that *oxygen is a necessary agent* concerned in the process of transformation that the sugar undergoes during the arterialization of blood that retains its living properties, or that has not as yet undergone spontaneous coagulation. It is, indeed, with great care that I have now, upon numerous occasions, repeated these experiments, and the uniform results that I have obtained, enable me confidently to advance the following conclusion. "*If right ventricular blood, or blood containing animal sugar, be made to traverse the capillaries of dead lungs inflated with air, immediately on its removal from the animal, and before coagulation has taken place, the sugar is as much destroyed as if it had passed through the pulmonary capillaries of the living animal; whilst if, on the contrary, the fibrine have separated by spontaneous coagulation, and the serum and corpuscles alone be employed, not the slightest disappearance of sugar is in this case to be observed.*" So that it is only, as it were, in *living blood*—blood before its spontaneous coagulation has taken place—that oxygen is capable of effecting the metamorphosis or destruction of sugar; for immediately that the last act of vitality has been performed, or that its fibrine has undergone spontaneous separation, the sugar ceases to be subjected to the influence of oxygen, until, as I shall presently point out, *incipient decomposition of the blood has set in.*

From the rapidity with which blood undergoes coagulation after its removal from the animal, it has necessarily happened, in some of my experiments on this subject, that the fibrine has undergone a partial separation before the injection through the pulmonary capillaries could be effected. As the result of these experiments, and likewise others in which the injection has been purposely delayed, I have noticed, also, what might have been antecedently expected, that the nearer the blood approaches the living condition, on exposure to contact with oxygen in the capillaries of the artificially inflated lungs, the

more complete is the destruetion of its saecharine constituent; whilst, in other words, the longer the period that elapses from its removal, the less the influenee that exposure to oxygen is eapable of producing.

Now, if the metamorphosis or destruction of sugar in the blood had been owing to the *direct chemical action* of oxygen, it certainly does not appear elear why it should not have made its disappearance *after* as well as *before* coagulation had taken plaee, espeeially as the temperature was maintained at an equal degree in each. We are, therefore, naturally led to infer that the presence of fibrine plays an essential and intermediate part. Indeed, during the existence of the fibrine in a soluble state, the blood still retains its vital characteristic, and is susceptible of undergoing molecular changes on contact with oxygen; which molecular ehanges, I think I shall be able to show, are instrumental in secondarily inducing the destruction of sugar.

If we first look to the ordinary chemical bearings of saccharine matter out of the animal economy, we find that when alone or in a state of purity it may be preserved for an indefinite period, without undergoing appreciable alteration, and that it is not susceptible of oxidation, except under the influence of strong chemical reagents; but that if placed in contact with a body in a state of molecular change, it is with extreme facility metamorphosed, or resolved into other compounds, by a process which falls under the popular designation of fermentation. When in eontact with the growing vegetable cells of the *Torula cerevisiæ*, it is the aleoholic fermentation that is excited; whilst, in contact with a decomposing azotized substanee, one atom of sugar ($C_{12}H_{12}O_{12}$) is with a simple alteration of its elements resolved into two atoms of lactic acid ($C_6H_6O_6$).

As, then, sugar is a substance that manifests so little susceptibility of direct oxidation in its ordinary chemical bearings; and as it is with such extreme facility metamorphosed when in contaet with an azotized principle whose elementary particles are in a state of change; chemical analogy alone would certainly induee us to look upon the latter as being the more probable proeess of physiological destruction, espeeially when we take into eonsideration that no where do we meet with such a eonstant series of molecular changes taking plaee as amongst the azotized eonstituents of the living animal.

It may be said, however, that the molecular changes occurring in the capillaries of the pulmonary organs—the chief seat of destruction of sugar in the animal economy—are not those of decomposition; but, if the changes of destruction or decomposition are capable of exciting this process of fermentation, why may not the changes necessarily incident on the elaboration or building up of these nitrogenized compounds effect the same? We, indeed, I think, are compelled to admit that they do, in order to interpret aright the foregoing experiments that I have referred to, upon the artificial arterialization of *fibrinated* and *defibrinated* blood. In these experiments it was found, that during the aëration of blood which still retained its fibrine, and might be regarded as in a living condition, the sugar largely disappeared; whilst in blood that had separated from its fibrine, and had lost its vitality, no such destruction of its saccharine constituent was observed. In the first instance, the nitrogenized elements of the blood were capable of undergoing the normal processes of elaboration or assimilation, on contact with oxygen, as in the living animal: in the latter, they had lost their capacity for these organizing changes, and there merely remained the ordinary chemical or physical action of oxygen on the colouring contents of the corpuscles.

It is not, moreover, only during the process of respiration, or in the pulmonary organs, that the metamorphosis of sugar is effected in the animal system; for I have already adduced experimental evidence to show, that the small amount of saccharine matter which escapes destruction in the lungs and impregnates arterial blood, continues to disappear (although at a far diminished rate), during the transit of this fluid through the general or systemic capillaries; so that the blood returning *from them* gives a still less reaction than that which was going *to them*, and in some of them—for instance, those of the chylo-poietic viscera—the sugar usually undergoes a total or complete destruction.

The fact that the metamorphosis of sugar is carried on in the systemic capillaries, and with greater activity in those of the chylo-poietic viscera than in the others, I look upon as a point of extreme interest and importance; and, I would ask, may we not reasonably attribute this metamorphosis

to a process analogous to fermentation induced by the molecular changes of nutrition? No one, I think, will hesitate to admit, that much more rapid and active changes are going on in the capillaries of the abdominal viscera than in other parts of the system at large; and this would at once account for the more complete transformation of sugar that is there observed.

These views, then, which have been derived from observation and experiment on the living and dead animal, give an explanation of the nature of the physiological destruction of sugar, which is perfectly consistent, and even analogous with what has been known for years past concerning the bearings of saccharine matter out of the animal economy. It is, indeed, only applying one of the principles of organic chemistry to the explanation of phenomena that belong to physiology. Out of the living system, it is well known that if glucose or grape sugar be placed in contact with caseine in a state of decomposition, (which implies molecular change,) it is resolved, by a process of fermentation, into lactic acid. In the living system, it would appear that a precisely similar transformation is induced by the molecular changes of assimilation and nutrition. In the one case the process is excited by the destruction or dissolution, in the other by the elaboration or building up of nitrogenized compounds.

If the saccharine matter of the animal economy really undergo this process of lactic acid fermentation, induced by the molecular changes of life, it next follows that we ought to meet with lactic acid as a constituent of the animal system; and, as the transformation chiefly takes place during the act of arterialization, we should especially look for its presence in arterial blood. I have carefully examined five specimens of arterial blood with this view; and although in the first, I obtained (on adopting the ordinary process recommended for this analysis) microscopic crystals closely resembling those of lactate of lime, figured in the plates accompanying Lehman's 'Physiological Chemistry,' yet I have not since been able to meet with them again. But the detection of lactic acid, when present in small quantity, is a process attended with considerable difficulty; and, I think, we have sufficient proof that it exists in arterial blood, in the fact that it is separated from it by the secreting follicles of the stomach, and by the muscular

tissue or flesh of animals. Chemists are now satisfactorily of accord in admitting the presence of lactic acid as a pretty abundant constituent of gastric juice and the juice of flesh. Sugar, therefore, which is normally a constant ingredient of right ventricular blood, principally disappears during the act of arterialization; and the lactic acid, into which it would appear converted, in the manner I have pointed out, is separated from this arterialized blood in the stomach and in the muscular tissue of animals.

It is well known, as regards the lactic acid fermentation, that the presence of an alkali favours or accelerates, whilst that of an acid retards or checks this process. Now, in collecting all the experimental evidence that suggested itself to me concerning the nature of the destruction of saccharine matter in the animal economy, I have injected carbonate of soda and phosphoric acid into the circulation, and, as the following details will show, the results I obtained were perfectly in accordance with the views that have been entertained on this subject. In the one case, I removed a small quantity of blood from the carotid artery of a black and tan terrier dog, and after observing that it communicated the usual small reaction of saccharine matter, I exposed the jugular vein, and injected into it about an ounce of the dilute phosphoric acid of the London Pharmacopœia. A second quantity of blood was removed from the same carotid artery, and this was now so largely impregnated with sugar that it communicated nearly as strong a reaction as right ventricular blood. It is worthy of remark, that the injection produced a faintly perceptible acid reaction of the blood. The animal manifested a considerable amount of disturbance, vomiting the contents of its stomach, voiding its fæces, and breathing in a hurried and laborious manner. It was afterwards affected with complete paralysis, first of the hind extremities, then of the fore, and subsequently died during the night. In the other case, 100 grains of the crystallized carbonate of soda, dissolved in 11 drachms of water, were similarly injected into the jugular vein of a dog, blood being removed for examination from the carotid artery before and after the operation. The two specimens of blood yielded, on analysis, a similar reaction, corresponding with that of ordinary arterial blood. The injection

produced some amount of disturbance, but the animal perfectly recovered in the course of a few days.

These two experiments, therefore, fully accord with the results that might have been anticipated upon the views that have been entertained. The blood is normally alkaline, and thus already in a condition favorable for the metamorphosis of sugar. The introduction of an alkali did not alter the rapidity of the process of saccharine destruction. Immediately, however, that the normal alkalinity was overcome by the injection of phosphoric acid, the metamorphosis ceased to be accomplished to its previous extent.

If we now direct our attention to the examination of the changes that occur in blood normally impregnated with saccharine matter, during spontaneous coagulation and whilst decomposition is taking place, we shall meet with some exceedingly interesting facts, which, I am not at all aware, have been by any one hitherto adverted to, and some of which considerably perplexed me in my analyses, until I became acquainted with them as the results of repeated observation. I have already shown, that whilst right-ventricular blood is susceptible of undergoing the molecular changes of life, exposure to the influence of oxygen effects a more or less complete metamorphosis or destruction of its contained sugar; and we have now to notice the results that the molecular changes of decomposition, and even of spontaneous coagulation, are capable of producing.

On collecting blood from the right ventricle of a healthy animal, placing it aside, so as to allow it to separate into clot and serum, and examining these on the following day; we find, that whilst the serum gives indications of being largely impregnated with saccharine matter, the clot communicates a scarcely traceable reaction. The details of the following observation, which I have repeatedly confirmed, will serve to show more explicitly what has just been stated.

About two ounces of blood having been collected from the right ventricle of a dog that had just been sacrificed for another purpose, it was placed aside until the following day, and allowed to undergo spontaneous coagulation. Two drachms of the serum were then taken, and found to yield an abundant indication of the presence of sugar. The whole of the clot that

had separated from the two ounces of blood was also, after being wiped with bibulous paper, carefully analysed in a similar manner, and gave only just a perceptible trace of saccharine reaction.

Now, as the clot is moist, and remains to a certain extent infiltrated with the serum from which it has separated, it certainly would appear from the above observation, that even the molecular changes arising from the spontaneous coagulation of the blood are sufficient to effect the metamorphosis or destruction of normal animal sugar. And this conclusion is strengthened by the fact, that in diabetic blood the saccharine matter does not seem to disappear in a similar manner. For instance, blood that has been removed from one of the veins of the arm of a diabetic patient has been allowed to undergo spontaneous coagulation, and although the serum has given about the same reaction as that of right-ventricular blood obtained from the healthy animal, yet the clot has also communicated a pretty abundant saccharine reaction:—a phenomenon which fully coincides with other facts to be presently adverted to,[1] and which appears to show that the sugar impregnating the blood of a diabetic patient does not enjoy the same susceptibility or facility of metamorphosis as the healthy variety. Whatever, however, the explanation, the fact remains unaltered: in the one case, the sugar completely or almost completely disappears in the clot; in the other, it is present to a considerable extent.

Under the changes attending the decomposition of the blood, normal animal glucose is very readily and rapidly metamorphosed or destroyed. On exposing, for example, healthy right-ventricular blood in contact with air, its azotised constituents, more or less rapidly, according to the temperature, undergo decomposition; and precisely in proportion to the activity of this decomposition, is the rapidity of the transformation of the glucose that is present. During the warm weather of the summer months I have found that usually in three of four days the sugar has entirely disappeared; and when this disappearance is complete, *the blood has assumed an acid reaction.*

The fact that right-ventricular blood becomes acid under decomposition, I observed nearly two years since; and I looked

[1] These facts I first noticed on examining the blood of a diabetic patient, under Dr. Barlow's care, in Guy's Hospital, during the summer of 1854.

upon it as exceedingly indicative of the nature of the transformation that the sugar underwent; for in blood, free or almost free from this principle, such as that obtained from the jugular vein, decomposition does not disturb the natural alkalinity of this fluid. On afterwards mentioning this fact to M. Bernard, of Paris, I discovered that he also had recently noticed the same phenomenon, without, as far as I am informed, having hitherto published any statement of it. The acidity which blood impregnated with saccharine matter thus acquires on decomposition, I attribute to the formation of lactic acid under the influence of the molecular changes that have been taking place subsequently to its death. Certain it is, that it cannot be due to carbonic acid, for the reaction remains after exposure to a boiling temperature.

The disappearance of sugar in right-ventricular blood during decomposition does not depend on the amount of surface exposed to the oxygen of the air (except in so far as this agent is concerned in exciting the putrefaction of the animal matters it contains), for the saccharine matter of blood, placed in an open test-tube, disappears just as rapidly as in that which has been exposed in an open saucer. All that is requisite, is slight exposure to the contact of oxygen, so as to excite a process of decomposition in the azotised elements of the blood; and through this, the destruction of sugar is, as it were, secondarily effected. If the air be carefully excluded, as by placing the blood immediately on removal in a closely-stoppered bottle, and accurately filling it, no signs of decomposition are, for a long time, to be observed, and under these circumstances the sugar also remains. The following details of an observation, which may be by anyone repeated, will serve to substantiate the statements that have been made.

June 21st, 1854.—Some blood having been collected from the right ventricle of a healthy dog that had just been sacrificed, one portion was placed in an open vessel, and another in a bottle that was filled and afterwards securely stoppered. At this period it presented its usual alkaline character, and yielded a strong saccharine reaction with the appropriate tests.

June 22d.—Blood in the open vessel examined; reaction similar to yesterday.

June 23d.—The blood in the open vessel now smelt strongly from putrefaction; and before and after coagulation by heat

gave an acid reaction to test-paper. Examined analytically for sugar, it was found to have lost all trace of this ingredient. The stopper was now removed from the other vessel, and its contents were found in precisely the same condition as when first removed from the animal, as regards its saccharine and other qualities.

June 24th.—The blood in the stoppered bottle having been exposed to the air since yesterday, it now began to smell from decomposition, and gave no indication of the presence of sugar.

It is worthy of remark, that at the period this observation was made, the weather was exceedingly warm, and the blood underwent more than ordinarily rapid decomposition. Usually the sugar does not disappear under three or four days after the removal of the blood from the animal. I have moreover found that the sugar in the fluid parts of the blood disappears quicker when the fibrine and corpuscles are present, than when the serum alone is exposed; and in accordance with this, the blood in the one case presents signs of decomposition much sooner than in the other;—a fact that is easily intelligible from the greater amount of azotised elements present. I have even observed, in the same specimen of arterial blood—where there is on removal but a small amount of sugar present—that when the fibrine has been separated, and the serum and corpuscles left, on allowing these to repose in a large test-tube, so that the globules may subside to the lower stratum of the liquid, and the serum be left clear above, the latter has given traces of the presence of sugar, whilst it has entirely disappeared from the former.

It has already been shown, that notwithstanding the oxygen of the atmosphere is capable of effecting the metamorphosis of sugar, when the blood is in a living condition, and its nitrogenized elements susceptible of undergoing the molecular changes coincident with life; yet, that immediately this vitality is withdrawn, contact with oxygen is no longer capable of inducing a similar destruction of sugar. If, however, blood normally impregnated with saccharine matter be allowed to remain until signs of incipient decomposition are observed, and the sugar is beginning to disappear, *exposure to a current of oxygen gas rapidly completes the total disappearance of all saccharine constituent.* To show this, it is only necessary to take some right-ventricular blood from a healthy animal, to

place it aside until it has begun to decompose and a portion of the sugar to disappear, and it will be found, that although oxygen exerted no influence upon it when in a fresh condition after death, yet that now a current of this gas passed through it for some minutes, effects (apparently by accelerating the molecular changes of decomposition in the nitrogenized principles present) the rapid destruction of the whole of the saccharine ingredient that remains. So that, in this fact we have a further illustration of the analogy that appears to exist in the nature of the metamorphosis of sugar as a vital process, and that which takes place chemically under the influence of an azotised compound whose particles are in a state of molecular transition. During life, the higher organic constituents of the blood are capable of undergoing the changes of assimilation on exposure to contact with oxygen, and there is a considerable destruction of sugar effected: for a short period after death the constitution of these azotised materials remains stationary and uninfluenced by oxygen; and with this there is a corresponding suspension of the transformation of sugar; but, finally, the animal matter of the blood on contact with oxygen —especially under the influence of a warm temperature—assumes a state of decomposition, the molecular changes of which again excite the destruction or metamorphosis of saccharine matter.

Upon reflecting on this transformation of saccharine matter into lactic acid in the animal economy, by a process analogous to that of fermentation, we cannot fail to appreciate the importance of the saccharine secretive function of the liver, which was some few years since discovered by the able and truly philosophic researches of M. Bernard, of Paris. Lactic acid is a normal ingredient, not only of the gastric secretion but also of the fluid which infiltrates the muscular tissue, or as it is called the juice of flesh. Now, it is only a certain class of animals—the vegetable feeders—which derive a supply of saccharine matter from their food; and, were it not that the others, the animal feeders, possessed an independent power of forming this substance, the normal source of lactic acid—an agent playing an important part in the animal processes—would be thus cut off.

When speaking of the effects of the spontaneous coagulation of fibrine on the saccharine constituent of healthy blood, I

stated that the sugar impregnating the blood of a diabetic patient did not seem to enjoy the same susceptibility of destruction as that which was met with in the right-ventricular blood of a healthy animal. And, if we refer to the effects produced by the decomposition of the azotised constituents of the blood, we are also led to a precisely similar conclusion. In normal right-ventricular blood exposed to the air and a warm temperature, I have shown that the sugar disappears in the course of a few days, whereas in diabetic blood exposed to similar conditions, I have found that the sugar does not disappear by two or three days so quickly. During August, 1854, I placed specimens of right-ventricular and diabetic blood side by side, and examined them carefully at daily intervals. In three days the sugar had completely disappeared from the right ventricular blood, whilst on the fifth day the diabetic blood still remained impregnated to a considerable extent with saccharine matter.

Hence, if I dared to hazard an opinion on the nature of that obscure disease, diabetes mellitus—the few observations that I have yet made on the blood of these patients would lead me to say, that there is a modification of sugar produced by the liver, which is not susceptible of undergoing the normal process of destruction or metamorphosis in the animal system, and which is eliminated on its arrival in the capillaries of the renal organs. The experiments of Bernard have shown, that if vegetable glucose (grape sugar) be injected into the general venous circulation, it is not destroyed in the system but is eliminated by the kidneys; whilst if it be injected into one of the veins of the portal system, and thus made to traverse the capillaries of the liver (so as to be converted into animal glucose), before entering the general circulation, it subsequently undergoes destruction in the system and does not appear in the urine. Diabetic sugar would, therefore, seem to bear a resemblance in its physiological relations to vegetable rather than to animal glucose. But I am now engaged in a series of experiments on this subject, which, with the information we possess at the present time, I would venture to hope, may some day lead to some definite conclusions concerning this long vexed pathological question.